PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ulf DE FAIRE Johan FROSTEGÅRD	Group Art Unit: 1644 Examiner: Sharon Wen
Serial No.: 10/599,934	Atty. Dkt. No.: EPCL:014US
Filed: May 31, 2007	
For: PHOSPHORYLCHOLINE CONJUGATES AND CORRESPONDING ANTIBODIES	Confirmation No.: 6769

CERTIFICATE OF ELECTRONIC TRANSMISSION

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February 17, 2011
Date

Steven L. Highlander

RESPONSE TO ELECTION OF SPECIES REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is in response to the Election of Species Requirement mailed on January 20, 2011, to which a response is due on February 20, 2011. No fees are believed to be due in connection with the filing of this response; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/EPCL:014US/10613208.

A **Listing of Claims** begins on page 2 of this response; **Remarks** begin on page 5.

LISTING OF CLAIMS

The following listing of claims replaces all previous listings or versions thereof:

1. (Canceled)

2. (Previously presented) A method for immunization and treatment of a human against atherosclerosis or an atherosclerotic related disease, the method comprising the step of administering to the human a pharmaceutical composition comprising an antibody preparation with specificity to a phosphorylcholine conjugate, wherein said preparation is a preparation of monoclonal antibodies with specificity for a phosphorylcholine conjugate or a subfraction of human immunoglobulin selected for the ability to bind to a phosphorylcholine conjugate.

3. (Previously presented) The method of claim 2 wherein the composition is administered by injection.

4. (Previously presented) The method of claim 2, wherein the phosphorylcholine conjugate comprises phosphorylcholine linked to a carrier via a spacer.

5. (Previously presented) The method according to claim 2, wherein the phosphorylcholine conjugate comprises phosphorylcholine linked to a protein carrier, optionally via a spacer.

6. (Previously presented) The method according to claim 5, wherein the protein carrier is KLH (keyhole limpet hemocyanin) or human serum albumin (HSA).

7. (Previously presented) The method according to claim 4, wherein the phosphorylcholine conjugate comprises phosphorylcholine linked to a latex bead, optionally via a spacer.

8. (Previously presented) A method of prophylactic or therapeutic treatment of a human being suffering from atherosclerosis or facing the risk of developing ischemic cardiovascular disease, whereby a therapeutically effective amount of an

antibody preparation with specificity to a phosphorylcholine conjugate is administered, wherein said preparation is a preparation of monoclonal antibodies with specificity for a phosphorylcholine conjugate or a subfraction of human immunoglobulin selected for the ability to bind to a phosphorylcholine conjugate.

9. (Previously presented) A method for assessing a human patient's risk of developing or progression of cardiovascular disease comprising assessing said patient's levels of antibodies reactive with the phosphorylcholine conjugate, wherein low levels of antibody reactive with the phosphorylcholine conjugate are predictive of the occurrence of cardiovascular disease in a healthy human patient.

10. (Previously presented) The method of claim 9, wherein the cardiovascular disease is ischemic cardiovascular disease.

11. (Previously presented) The method of claim 9, wherein the cardiovascular disease is atherosclerosis.

12. (Previously presented) The method of claim 9, wherein the patient's levels of IgM antibodies reactive with the phosphorylcholine conjugate are assessed.

13. (Previously presented) The method of claim 9, wherein the patient's levels of IgG antibodies reactive with the phosphorylcholine conjugate are assessed.

14. (Previously presented) The method of claim 9, wherein phosphorylcholine is linked to a carrier via a spacer.

15. (Previously presented) The method of claim 9, wherein the phosphorylcholine conjugate comprises-phosphorylcholine linked to a protein carrier, optionally via a spacer.

16. (Previously presented) The method of claim 15, wherein the protein is KLH (keyhole limpet hemocyanin) or human serum albumin (HSA).

17. (Previously presented) The method of claim 9, wherein the phosphorylcholine conjugate comprises-phosphorylcholine linked to a latex bead, optionally via a spacer.

18. (Previously presented) The method of claim 9, wherein the assay is an immunoassay.

19. (Previously presented) The method of claim 2, wherein said antibody preparation is a monoclonal antibody preparation.

20. (Previously presented) The method of claim 8, wherein said antibody preparation is a monoclonal antibody preparation.

21. (Previously presented) The method of claim 2, wherein the human that is immunized and treated is a human patient that has been determined to be at risk of developing or progression of cardiovascular disease by a method comprising assessing the human patient's level of antibodies reactive with a phosphorylcholine conjugate, wherein the level of antibodies reactive with a phosphorylcholine conjugate correlates negatively with the risk of developing or progression of cardiovascular disease in a healthy human patient.

22. (Previously presented) The method of claim 21, wherein the cardiovascular disease is atherosclerosis.

23. (Previously presented) The method of claim 21, wherein the human patient has been determined to be at risk of developing or progression of cardiovascular disease by a method comprising assessing the human patient's level of IgM antibodies reactive with a phosphorylcholine conjugate.

24. (Previously presented) The method of claim 21, wherein the human patient has been determined to be at risk of developing or progression of cardiovascular disease by a method comprising assessing the human patient's level of IgG antibodies reactive with a phosphorylcholine conjugate.

REMARKS

I. Status of the Claims

Claims 2-24 are pending in the application, and claims 7 and 9-18 stand withdrawn pursuant to a restriction requirement. Therefore, claims 2-6, 8 and 19-24 are under consideration. The examiner has now entered an election of species requirement against these claims.

II. Election with Traverse

The examiner is requiring election between (a) a preparation of monoclonal antibodies with specificity for a phosphorylcholine conjugate or (b) a subfraction of human immunoglobulin selected for the ability to bind to a phosphorylcholine conjugate, as presently recited in claims 2 and 8.

In response, applicants elect species (a), monoclonal antibodies with specificity for a phosphorylcholine conjugate, with traverse. Claims 2-6, 8 and 19-24 read on the elected species and are generic.

III. Traversal

The examiner identifies two species, namely (a) a preparation of monoclonal antibodies with specificity for a phosphorylcholine conjugate; and (b) a subfraction of human immunoglobulin selected for the ability to bind to a phosphorylcholine conjugate. In so doing, the examiner states that:

> The shared feature of the present invention is treating atherosclerosis with anti-phosphorylcholine (PC) antibody. The shared feature does not contribute over the prior art because it is obvious in view of Rose et al. (*Nature Medicine*

> 2003, 9:641-642, cited on IDS). Rose et al. proposed a role for PC-specific autoantibodies in slowing the progression of atherosclerosis by binding to oxidized low-density lipoprotein in the circulation; thereby clearing it from the circulation and making it unavailable for plaque formation (see Figure 1). Upon reading the teaching by Rose et al, one of ordinary skill in the art would have been motivated to treat atherosclerosis with anti-PC antibody. Furthermore, one of ordinary skill would have had reasonable expectation of success because antibody treatment has been well-established in the art at the time of the invention was made. Therefore, the shared feature was prima facie obvious to one of ordinary skill in the art and does not contribute over the prior art.

Applicant respectfully disagrees with the examiner's allegations.

First, applicant submits that the examiner has not fully and correctly identified the extent of the shared feature between the identified species. The full extent of shared feature is apparent from a reading of current claim 2:

> 2. A method for immunization and treatment of a ***human*** against atherosclerosis or an atherosclerotic related disease, the method comprising the step of administering to the ***human*** a pharmaceutical composition comprising ***an antibody preparation*** with specificity to a phosphorylcholine conjugate, wherein said preparation is a preparation of monoclonal antibodies with specificity for a phosphorylcholine conjugate or a subfraction of human immunoglobulin selected for the ability to bind to a phosphorylcholine conjugate.

Emphasis added. Therefore, when read in the full context of the claim, it is apparent that the identified species share the feature of treating atherosclerosis ***in humans*** by ***administration of an antibody preparation*** with specificity to a phosphorylcholine conjugate.

Second, applicant submits that the full extent of the shared feature between the two identified species is not rendered obvious by Rose *et al.* As will be discussed in more detail below, Rose *et al.* is ***solely*** concerned with tests conducted by vaccination of mice. Rose *et al.* neither discloses or renders obvious (i) the treatment of atherosclerosis by administration of any sort of antibody preparation; or (ii) the treatment of atherosclerosis in humans.

Both of the foregoing points are well-demonstrated by Rose *et al.*, page 642, 2nd col., lines 4-6 and 16-19 which, respectively, state that:

> Notably, ***pneumococcal immunization*** reduced atherosclerosis in LDL receptor-deficient ***mice***.
>
> .....
>
> ***Before seriously considering*** whether we can prevent atherosclerosis with a ***pneumococcal vaccine***, the function of antibodies to oxLDL ***must be defined in humans***.

Emphasis added. All of the data discussed in Rose *et al.* is derived from tests conducted in mice. The skilled person is explicitly taught by Rose *et al.* that one cannot yet "seriously consider" using its pneumococcal vaccine to treat atherosclerosis in humans, because of the undefined role of anti-oxLDL antibodies in humans.

In fact, Rose *et al.* also highlights further strong reasons for uncertainty about the role of antibodies raised against a pneumococcal vaccine in atherosclerosis, even in mice as tested. Rose *et al.*, at page 642, 2nd col., line 22 to col. 3, line 6 states that:

> Some oxLDL-specific antibodies do ***exactly the opposite*** of what was described by Binder et al; that is, they enhance the uptake of oxLDL by macrophages and ***accelerate atherosclerosis in a mouse model***.
>
> The issue may be ***further complicated*** by the presence of autoantibodies directed against T15 itself, described during early studies of the T15 antibody[8,9]. Autoantibodies against oxLDL antibodies may block the protective effect of oxLDL specific antibodies. Autoimmunity can be "good" or "bad", physiogenic or pathogenic, depending on the circumstances. ***It is important to understand the rules before we intervene***.

Emphasis added. Accordingly, there are yet further good reasons to conclude that, in light of the teaching in Rose *et al.*, the skilled person effectively has no idea whether using a pneumococcal vaccine, as suggested, would really be atheroprotective, either in mice or humans. Rose *et al.* is clear in stating that the "rules" for the role of the anti-oxLDL antibody types in atherosclerosis are simply not understood in mice, much less in humans, and there is capacity for autoantibodies to be harmful and promote atherosclerosis, and is explicit that one cannot "seriously consider" extrapolating its findings to humans.

Moreover, there are simply no data in Rose *et al.* to show any role for anti-oxLDL antibodies in the atherosclerotic process in humans, only clear doubts from the authors about (a) whether the observations are a valid demonstration of an atheroprotective effect in mice at all; and (b) whether one can seriously contemplate transferring observation taken from mice to humans.

All of the foregoing is in direct contrast to the examiner's unsupported assertion that, in light of Rose *et al.*, "one of ordinary skill would have a reasonable expectation of success." The explicit teaching in Rose *et al.* is that the skilled person would have had ***no reasonable expectation*** of success in treating atherosclerosis in humans by following its teachings. Thus, Rose *et al.* does not render it obvious to the skilled person that one could treat atherosclerosis in humans by any means.

Moreover, even if one of skill in the art had followed the teaching of Rose *et al.* and tried to implement its teaching in humans in the mere hope that some success might follow (which suggestion is denied), then it motivates them only to administer a "pneumococcal vaccine." The administration of a pneumococcal vaccine is clearly different than the administration of "an antibody preparation with specificity to a phosphorylcholine conjugate" as presently claimed. Additionally, a pneumococcal vaccine as taught by Rose *et al.* would clearly result in the production of a heterogeneous immune response to the large number of different immunogens presented by that complex vaccine. Accordingly, the use of a pneumococcal vaccine as taught by Rose *et al.* would clearly be expected to produce a very different effect on the immune system of a patient as compared to the administration of an antibody preparation having a defined binding specificity to PC conjugate as currently claimed, and the skilled person would not have considered the latter to be an obvious alternative to the former.

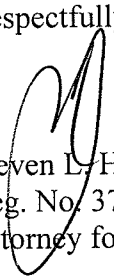
In sum, there is absolutely no motivation in Rose *et al.* to deviate from its teaching of using a pneumococcal vaccine, for example to arrive at the use of a PC conjugate alone as a vaccine, much less to abandon vaccination altogether and an instead administer an antibody preparation with pre-selected specificity to PC conjugate in the manner presently claimed. The use of a defined antibody preparation with pre-selected specific binding properties for PC conjugate, as presently claimed, is clearly distinct from, and non-obvious in light of, the "pneumococcal vaccine" as taught by Rose *et al.*

Accordingly, the skilled person would certainly not consider obvious from Rose *et al.*, nor have any reasonable expectation, that an antibody preparation with specificity to PC conjugate would be effective to treat atherosclerosis, even in mice and certainly not in humans. Thus, contrary to the examiner's allegation, Rose *et al.* did not render obvious the treatment of atherosclerosis in humans by the administration of an antibody preparation with specificity to a phosphorylcholine conjugate, as presently claimed. Thus, it flows that the feature shared between the two identified species is not obviated by Rose *et al.*, and thus the election of species is improper and should be withdrawn.

IV. Conclusion

The foregoing is believed to be a complete response to the January 20, 2011 action. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



Steven L. Highlander
Reg. No. 37,642
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201

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